REMARKS

In response to the action mailed January 24, 2005, Applicants amended claim 1 to specify that the acidic component is an organic acid and that the acidic component is effective to produce a pH in the environment of use that is below pH4 and to release NO or NO_2 ions that potentiate the patient's immune system against the pathogen. Support for these amendments can be found throughout the specification. See for example page 7, lines 10-11, page 7, lines 30-36,[1] page 3, lines 21-29,[2] page 4, lines 8-16,[3] page 8, line 14, and page 12, lines 6-7. See also page 26, lines 1-5, which indicates that nitrogen oxide complex-treated skin showed significant increases in immuno-competent cells expressing CD3, CD8, CD68 and neutrophil elastase and in the adhesion molecules which attract trafficking of the cells to the site, ICAM-1 and VCAM-1. Finally, page 29, lines 10-18 is explicit that,

> The promotion of apoptosis and recruitment of all the immunocompetent cells required for effective recognition of a pathogen by the immune system of a host, results from application of a preparation of a combination of nitrite or precursor of nitrogen oxides and an acidifying agent. Accordingly, these findings support a potential immunopotentiating effect of the combination of nitrite or other precursor of nitrogen oxides such as NO or NO_2 and a acidifying agent.

New claim 19 specifies that the acidic component consists essentially of organic acid, as supported by the acidic component in each of the specific examples.

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[1] Once at the infected cells the nitrogen oxide complex can facilitate programmed cell death, selectively in infected cells, which may then be taken up by phagocytes and antigen presenting cells leading to immune recognition of the previously hidden viral antigens. Once recognized, specific immunity will lead to destruction of all infected cells through cellular and humoural responses.

[2] We have now found inter alia that nitrite at concentrations of up to 4% in an inert carrier cream or ointment when mixed with an organic acid such as salicylic acid reacts to produce oxides of nitrogen which are effective in killing infectious organisms on the skin including fungi, yeast, bacteria and viruses. The combination of nitrite and acid causes mild erythema (redness) of the skin due to release of nitric oxides at the environment of use but this causes no significant inflammation.

[3] It has been found that although the healthy keratinocytes find the oxides of nitrogen toxic they do not die as they are relatively resistant to its effects. However, the surprising clinical results in our examples lead us to believe that virally infected cells are more susceptible to these effects, leading to destruction of the virally infected cells via a combination of toxicity leading to programmed cell death and potentiation of the immune response to the presence of the virus.

New claim 20 specifies that the pH at the environment of use is sufficiently high to potentiate the patient's immune system selectively against the bacterial, viral or fungal condition, as compared to normal patient cells. This claim is supported by the above-cited portions of the specification. Page 7, lines 34-36 provides,

> Once recognized, specific immunity will lead to destruction of all infected cells through cellular and humoural responses.

As noted, page 4, lines 8-16 says that virally infected cells are more susceptible to the invention than healthy cells (see footnote 3).

Claim 1 was rejected in the office action under 35 U.S.C. §102(b) as being anticipated by Mardi et al. (U.S. Patent No. 4,595,591).

Claim 1 includes the above discussed limitation concerning potentiation of the immune system. Nowhere does Mardi et al. disclose potentiation of the immune system. On the contrary, Mardi et al. discloses that it's composition mummifies tissue at column 3, line 66 to column 4, line 1, "[d]uring the reaction of the composition, the integumental proteins are immediately denatured in situ and the anatomical structure is fixed intravitally (mummified) without being altered or injured." At column 4, lines 41-44, Mardi et al. discloses "an advantageous embodiment of the invention, the aqueous solution has an acid equivalent of from about 8.0 to about 9.5 millimol/ml; besides this its pH-value preferably is below 0."

In short, the invention thus provides an immune-based attack on cells relying on apoptosis and other immune system processes rather than indiscriminate "fixing" or "mummification" of the cells disclosed in Mardi et al. Nor does Mardi et al. provide any teaching that would lead to immune potentiation that is selective for the bacterial, viral or fungal condition, as compared to normal patient cells, as provided in claim 20.

Further, claim 1 as amended specifies that the acidifying agent is an organic acid. Mardi et al. discloses compositions with nitric acid or nitrous acid as the acidifying agent. Although, in some of its compositions Mardi et al. uses combines oxidizable organic acids with nitric or nitrous acid, it is clear from Mardi et al.'s disclosure that nitric acid is always present as an acidifying agent to maintain the composition at a pH below 1. For that additional reason, Mardi

et al. does not anticipate amended claim 1 or claim 19. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Enclosed is a $225 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney's Docket No. 13227-002003.

Respectfully submitted,

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